Concerns and opportunities related to discontinuation of treatment in rheumatoid arthritis

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PART III
Treatment of rheumatoid arthritis during a pandemic


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Prospective study into COVID-19 like symptoms in patients with and without immune-mediated inflammatory diseases or immunomodulating drugs

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Letter to the Editor

With the arrival of SARS-CoV-2, it was asked whether our patients with immune mediated inflammatory disorders, or who had an organ transplantation (IMDT patients) and/or use immunosuppressive medication (imed) are more susceptible to SARS-CoV-2 infection and/or a severe COVID-19 disease course. In the earliest reports on COVID-19, such patients were rarely described. Most reports were retrospectively collected, in various case series or cohorts without a control group.(1-3) The Infection and Immunomodulation Inventory Initiative (Dutch acronym: IENIMINI) cohort study was started March 10th 2020 to prospectively register self-reported periods of illness with COVID-19 like symptoms (CLS) (see questionnaire in *supplementary table 1*) and compare these between IMIDT patients with and without imed and controls as selected from the hospital database of the Leiden University Medical Center (LUMC) in March 2020. Patients were defined as being in outpatient care at the outpatient clinic for rheumatology, gastroenterology, pulmonology and/or nephrology and having an autoinflammatory or autoimmune disease or having had a solid organ transplantation with or without imed (verified from the medical records after participant's informed consent). Controls were persons who had visited these outpatient clinics in the previous three years and were discharged but did not have an IMIDT.

Of the 8670 individuals approached, 2110 with IMIDT and 1067 controls agreed to participate (see baseline characteristics in *supplementary table 2*) and differences between the non-repliers and repliers/participants in *supplementary table 3*). The most prevalent diagnoses among the participants from the IMIDT group were ulcerative colitis, Crohn's disease and seropositive rheumatoid arthritis (see supplementary table 4). Between March and July 2020, 554 (33%) IMIDT patients and 299 (35%) controls recorded an illness episode with at least one symptom, mostly mild with a median (interquartile range, IQR) duration of four (3-6) days in both IMIDT patients and controls. Sixteen (6%) IMIDT patients with immunosuppressive medication (imed), 8 (3%) IMIDTs without imed and 5 (2%) controls were hospitalized with CLS (p=0.8). Logistic regression analysis showed that female gender (Odds Ratio (OR) 1.45 95% confidence interval (CI) 1.15;1.82), lung disease (OR 1.50 95%CI 1.20;1.88) and wearing a face mask (then not yet mandatory) (OR 1.42 95%CI 1.13-1.77) were independently associated with a higher risk of experiencing CLS, whereas older age and use of imed were associated with a lower risk (see *table 1*).

Table 1. Univariable & multivariable analysis of variables associated with having CLS or not (OR with 95% CI)

	Data from n	Univariate	Multivariate*
Sex, female	2546	1.89 (1.58;2.25)	1.45 (1.15;1.82)
Age	2546	0.97 (0.96;0.97)	0.96 (0.96;0.97)
BMI	2391	0.99 (0.97;1.01)	1.00 (0.98;1.03)
Smoking (current)	2463	1.35 (1.02;1.78)	1.05 (0.74;1.50)
Daily alcohol use	2416	0.84 (0.71;1.00)	1.20 (0.96;1.50)
Solid organ transplantation	2546	0.74 (0.54;1.03)	0.79 (0.47;1.35)
IMIDT without imed†	2546	1.00 (0.82;1.23)	0.94 (0.72;1.24)
IMIDT with imed†	2546	0.79 (0.65;0.97)	0.68 (0.51;0.91)
Use of oral corticosteroids	2546	0.84 (0.66;1.06)	1.44 (0.95;2.20)
Self-reported Diabetes Mellitus	2381	0.69 (0.50;0.96)	0.89 (0.58;1.36)
Self-reported lung disease	2396	1.30 (1.09;1.54)	1.50 (1.20;1.88)
Self-reported heart disease	2399	0.85 (0.69;1.04)	1.09 (0.83;1.43)
Influenza vaccination**	2415	0.71 (0.60;0.84)	0.96 (0.76;1.21)
Physical contact with family***	2220	1.47 (1.22;1.78)	1.22 (0.98;1.53)
Visiting other people (not family)	2205	1.26 (1.05;1.51)	0.96 (0.77;1.20)
Wearing a face mask	2196	1.46 (1.20;1.76)	1.42 (1.13;1.77)
Close contact (at work)	2180	1.65 (1.34;2.03)	1.27 (0.97;1.66)
Good adherence to lockdown rules	2245	1.17 (0.41;3.29)	2.46 (0.65;9.38)
Working outside the house	2435	1.39 (1.16;1.68)	0.92 (0.71;1.20)

Abbreviations: BMI=body mass index; CI= confidence intervals; CLS=COVID-19 like symptoms; IMIDT= with immune mediated inflammatory disorders or transplant organ; n=number; OR=odds ratio.
* number of observations: 1835
** in autumn 2019
*** physical contact specified as 'holding/shaking hands, hugging etcetera'
† control group = reference group

Thus, we found a similar incidence of COVID-19 like symptoms in IMIDT patients (with or without immunosuppressive medication) and controls. However, IMIDT patients on imeds with CLS had a slightly higher risk to be admitted to hospital, which may suggest worse symptom severity or an estimated greater risk of deterioration. We collected only self-reported symptoms mostly for logistical reasons. With 22% of participants reporting COVID-19 like symptoms, we may have overestimated the occurrence of COVID-19 and also included symptoms of influenza (season ended in March) and common colds, which in turn may have been over-reported during the anxious times of the 'first wave' of COVID-19. But since SARS-CoV-2 infection often results in mild flu like symptoms only, we may in fact have come closer to the true infection rate than what has been reported in earlier observations based on hospitalizations and testing of worse cases.

A relatively low response rate (37%) to our invitation to participate in this study means that there is a possibility of selection bias, the effect of which we cannot estimate.

In conclusion, between March and July 2020, IMIDT patients, whether or not taking imeds, did not show an increased risk of reported COVID-19-like symptoms compared to controls. In our population, continuing immunosuppressant drugs as long as not ill, while following the Dutch COVID-19 rules, appears to be safe.

References

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